Dow AgroSciences LLC
9330 Zionsville Road
Indianapolis, IN 46268

201-14945

Dow AgroSciences

Ms. Marianne L. Horinko
Administrator
U.S. Environmental Protection Agency
P.O. Box 1473
Merrifield, VA 22116

Dear Ms. Horinko:

CHEMICAL RIGHT TO KNOW – HPV CHALLENGE PROGRAM

On behalf of Dow AgroSciences LLC, I am pleased to submit the robust summaries in IUCLID format for 3,4,5,6-tetrachloro-2-pyridine carbonitrile (Cas No.: 17824-83-8). As requested, the test plan has been posted onto the U.S. HPV Chemical Tracking System. All documents are in Adobe Acrobat (pdf) files.

We understand this information will be posted on the Internet for comments for a period of 120 days. Please forward comments to me at the following address:

Ms. Gail M. Garvin
Dow AgroSciences LLC
9330 Zionsville Road
Indianapolis, IN 46268

Sincerely,

Gail M. Garvin
Global Environmental, Health & Safety Specialist
(317) 337-3609

201-14945A

HIGH PRODUCTION VOLUME (HPV)

CHEMICAL CHALLENGE PROGRAM

TEST PLAN

For

3,4,5,6-TETRACHLORO-2-PYRIDINE CARBONITRILE

Prepared by:

The Dow Chemical Company

December 11, 2003

PLAIN ENGLISH SUMMARY

This test plan addresses 3,4,5,6-tetrachloro-2-pyridine carbonitrile (CAS No. 17824-83-8). Existing data are summarized. No additional data are needed under the HPV Challenge Program.

EXECUTIVE SUMMARY

The Dow Chemical Company hereby submits for review and public comment the test plan for 3,4,5,6-tetrachloro-2-pyridine carbonitrile under the Environmental Protection Agency's (EPA) High Production Volume (HPV) Chemical Challenge Program. It is the intent of The Dow Chemical Company to use a variety of existing data and scientific judgment/analyses to adequately characterize the SIDS (Screening Information Data Set) human health, environmental fate and effects, and physicochemical endpoints for this chemical.

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TEST PLAN FOR 3,4,5,6-TETRACHLORO-2-PYRIDINE CARBONITRILE

I. INTRODUCTION

The Dow Chemical Company has committed voluntarily to develop screening level human health effects, environmental effects and fate, and physicochemical test data for 3,4,5,6-tetrachloro-2-pyridine carbonitrile under the Environmental Protection Agency's (EPA's) High Production Volume (HPV) Challenge Program (Program).

This plan identifies the chemical and its CAS number and identifies existing data of adequate quality for the chemical to develop screening level data for the chemical under the Program. The objective of this effort is to identify sufficient test data and/or other information to adequately characterize the human health and environmental fate for the chemical in compliance with the EPA HPV Program. Physicochemical data that are requested in this program will be provided.

II. DESCRIPTION OF 3,4,5,6-TETRACHLORO-2-PYRIDINE CARBONITRILE

A. The Chemical

3,4,5,6-tetrachloro-2-pyridine carbonitrile (CAS No. 68412-40-8) is a member of a group of chemicals known as chloropyridines, used in the production of chlorinated pesticides. The safe handling information for this stream will be determined from existing data for the material and other structurally similar materials which have been studied to provide safe handling information.

III. TEST PLAN RATIONALE

A. Classification of the Chemical as a Site-Limited Intermediate

1. Requirements

Classification of 3,4,5,6-tetrachloro-2-pyridine carbonitrile as a site-limited intermediate under the EPA HPV program is dependent upon a number of criteria outlined by EPA. The Dow Chemical Company asserts that this derivative stream should be regarded as a site-limited intermediate, based on satisfaction of these criteria. In the following paragraphs, we have provided information on the extremely limited potential for exposure during manufacturing, transport, consumption and use.

2. Satisfaction of Requirements

a. Review of Manufacture / Transport / Consumption:

3,4,5,6-Tetrachloro-2-pyridine carbonitrile is produced in a single facility within The Dow Chemical Company's Freeport Operations Site located in Freeport, TX. 3,4,5,6-Tetrachloro-2-pyridine carbonitrile is contained and consumed within the same facility in the production of pesticides.

b. Environmental Fate

The potential for environmental exposure to 3,4,5,6-tetrachloro-2-pyridine carbonitrile is neglible. There are no releases to water or land unless a major plant upset occurred.

Since 3,4,5,6-tetrachloro-2-pyridine carbonitrile is consumed entirely as an intermediate, the downstream processing/use will result in yet a smaller fraction of air emissions that described above during manufacturing. As the residual level of 3,4,5,6-tetrachloro-2-pyridine carbonitrile in downstream products is typically non-detectable and the downstream products are converted into other products, there is essentially no potential for environmental exposure through its use.

c. Human Exposure

The potential for human exposure is also extremely low. Due to the very corrosive nature of 3,4,5,6-tetrachloro-2-pyridine carbonitrile, personal protective equipment is worn during production, maintenance, distribution and processing to ensure no personal contact. Personal protective equipment includes goggles, face shield, hard hat, protective full rubber suit and boots. If maintenance is required in areas where 3,4,5,6-tetrachloro-2-pyridine carbonitrile had been present, the protective equipment would include a full rubber suit, face shield, goggles, and a full face respirator.

3. Conclusion

The Dow Chemical Company believes that the information above fully satisfies the EPA's criteria on site limited intermediates. Further, the above information suggests that there appears to be little additional action that could be taken to prevent any further exposure as the exposure simply doesn't occur.

B. Human Health Effects

There are six mammalian toxicity endpoints in the HPV Program:

- Acute Toxicity
- Repeated Dose Toxicity
- Genetic Toxicity *In Vitro*
- Genetic Toxicity *In Vivo*
- Reproductive Toxicity
- Developmental Toxicity

In an effort to reduce animal testing and to leverage existing data, published and unpublished data for 2,3,4,5,6-pentachloropyridine (CAS No. 2176-62-7), as detailed in the attached Robust Summaries, will be used as a surrogate to satisfy the requirements of all required mammalian testing not already available for 3,4,5,6-tetrachloro-2-pyridine carbonitrile. These two materials have been analyzed through a qualitative structure-activity relationship (QSAR) program. Results of the QSAR indicate that the materials are likely to behave in a similar fashion, and thus the data detailed for pentachloropyridine are conservatively estimated to provide adequate protection from the carbonitrile. Additional testing would be unlikely to change safe handling recommendations for the carbonitrile. Thus, the attached Robust Summaries provide adequate data to characterize the human health effects endpoints under the Program.

C. Ecotoxicity

There are three aquatic toxicity endpoints in the HPV Program:

- Acute Toxicity to Fish
- Acute Toxicity to Aquatic Invertebrates
- Toxicity to Algae (Growth Inhibition)

In an effort to reduce testing and to leverage existing data, published and unpublished data for 2,3,4,5,6-pentachloropyridine (CAS No. 2176-62-7), as detailed in the attached Robust Summaries, will be used as a surrogate to satisfy the requirements of all required ecotoxicity testing.

D. Environmental Fate

Predictive models were used to develop meaningful data for chemicals that are gaseous at relevant environmental temperatures and pressures. The environmental fate data include:

- Photodegradation
- Stability in Water (Hydrolysis)
- Transport and Distribution (Fugacity)
- Biodegradation

In an effort to reduce testing and to leverage existing data, published and unpublished data for 2,3,4,5,6-pentachloropyridine (CAS No. 2176-62-7), as detailed in the attached Robust Summaries, will be used as a surrogate to satisfy the requirements of all required environmental fate testing.

E. Physicochemical Properties

The physicochemical properties include:

- Melting Point
- Boiling Point
- Vapor Pressure
- Octanol/Water Partition Coefficient

Data for physicochemical properties will be summarized from various resources and detailed in the attached Robust Summaries.

IV. TEST PLAN SUMMARY

This test plan is expected to provide adequate data to characterize the human health effects and environmental fate and effects endpoints under the Program.

For reasons indicated in the above paragraphs, we do not believe additional data needs to be generated beyond the studies listed. Due to the nature of the chemical; the manner in which the chemical is manufactured, distributed, processed and used, the product stewardship measures taken to prevent exposure; and existing human/environmental data, we believe that our workers, the public and the environment are well protected from exposure to 3,4,5,6-tetrachloro-2-pyridine carbonitrile.

REFERENCES

1. US EPA. 1999. Determining the Adequacy of Existing Data. OPPT, EPA.

2. DEREK Version 7.0 for Windows, Lhasa LTD, 2003.

201-14945B

IUCLID

Data Set

Existing Chemical	:	ID: 2176-62-7
CAS No.	:	2176-62-7
Common name	:	2,3,4,5,6-Pentachloropyridine
Producer Related Part		
Company	:	The Dow Chemical Company
Creation date	:	20.05.2002
Substance Related Part		
Company	:	The Dow Chemical Company
Creation date	:	20.05.2002
Memo		
Printing date	:	05.06.2002
Revision date		
Date of last Update	:	05.06.2002
Number of Pages	:	18
Chapter (profile)		
Reliability (profile)		
Flags (profile)	:	???

1.0.1 OECD AND COMPANY INFORMATION

Type
Name Dow AgroSciences
Partner
Date
Street 9330 Zionsville Road
Town Indianapolis, IN 46268-1189
Country United States
Phone
Telefax
Telex
Cedex
04.06.2002

Type :
Name : The Dow Chemical Company
Partner :
Date :
Street : 2020 Dow Center
Town : 48674 Midland, Michigan
Country : United States
Phone :
Telefax :
Telex :
Cedex :
20.05.2002

1.0.2 LOCATION OF PRODUCTION SITE

Name of Plant
Street
Town Freeport, TX
Country United States
Phone
Telefax
Telex
Cedex
04.06.2002

Name of Plant
Street
Town Pittsburg, CA
Country United States
Phone
Telefax
Telex
Cedex
04.06.2002

1.0.3 IDENTITY OF RECIPIENTS

Name of recipient The Dow Chemical Company
Street

Town	:	Freeport, TX
Country	:	United States
Phone	:	
Telefax	:	
Telex	:	
Cedex	:	

04.06.2002

1.1 GENERAL SUBSTANCE INFORMATION

Substance type	:	inorganic
Physical status	:	solid
Purity	:	> 99 % w/w
Test substance	:	Molecular formula = C5Cl5N Molecular weight = 251.3 Substance Type = organic Physical status = white solid Odor = sharp pyridine-like

04.06.2002

1.1.0 DETAILS ON TEMPLATE

1.1.1 SPECTRA

1.2 SYNONYMS

:Pentachloropyridine
20.05.2002

PCP
04.06.2002

1.3 IMPURITIES

CAS-No	:	
EINECS-No	:	
EINECS-Name	:	2,5,6-trichloro-3-pyridinecarboxylic acid
Contents	:	% w/w

04.06.2002

CAS-No	:	2808-86-8
EINECS-No	:	
EINECS-Name	:	Tetrachloropyridine
Contents	:	= .4 % w/w

04.06.2002

1.4 ADDITIVES

1.5 QUANTITY

Production during the

last 12 months
Import during the last 12 months
Quantity produced 10 - 50 tonnes in
04.06.2002

1.6.1 LABELLING

1.6.2 CLASSIFICATION

1.7 USE PATTERN

Type : type
Category : Non dispersive use
Remark : 1) 75 % used in the manufacturing of Symtet
2) 24.9 % sent to Freeport, Texas
3) 0.1% sent to external customers
04.06.2002

Type type
Category Use in closed system
04.06.2002

Type : industrial
Category : Agricultural industry
04.06.2002

Type : industrial
Category : other: pharmaceutical industry
04.06.2002

Type : use
Category : Intermediates
04.06.2002

1.7.1 TECHNOLOGY PRODUCTION/USE

1.8 OCCUPATIONAL EXPOSURE LIMIT VALUES

Type of limit other: Dow AgroSciences Industrial Hygiene Guide
Limit value 7 mg/m3
04.06.2002

1.9 SOURCE OF EXPOSURE

Memo Sources of Exposure
Remark Sampling conducted using Proper Protective Equipment per the MSDS recommendation.
This chemical is produced in Pittsburg, California and is shipped to Freeport, Texas. Therefore, chemical is present at two sites. The chemical known as PCP is an intermediate in the production of Symtet and Starane

Herbicide. Chlorine and Picolines are reacted in a vapor phase reactor followed by a series of liquid phase reactors. This material is then distilled with the PCP product stored in a tank prior to loading into a rail car. The unreacted material is recycled back to the reactors and reprocessed. The system is fully contained with no atmospheric vents. Vents are collected and sent to a vent condenser followed by thermal incineration or caustic scrubber. The scrubber effluent is sent to a Chlorinolysis facility for treatment and disposal. We have in process flow meters that perform material balances to ensure and track that PCP volumes do not escape into the environment. PCP is present in the Symtet intermediate at the 0.1 - 0.6 wt% level. PCP is not present in the end-use products of Garlon (Triclopyr) or Chlorpyrifos. PCP is also present in N-Serve 24 at the 0.2 - 0.44 wt% levels. This is an end use product.

04.06.2002

1.10.1 RECOMMENDATIONS/PRECAUTIONARY MEASURES

1.10.2 EMERGENCY MEASURES

1.11 PACKAGING

1.12 POSSIB. OF RENDERING SUBST. HARMLESS

1.13 STATEMENTS CONCERNING WASTE

1.14.1 WATER POLLUTION

1.14.2 MAJOR ACCIDENT HAZARDS

1.14.3 AIR POLLUTION

1.15 ADDITIONAL REMARKS

1.16 LAST LITERATURE SEARCH

1.17 REVIEWS

1.18 LISTINGS E.G. CHEMICAL INVENTORIES

2.1 MELTING POINT

Value	:	= 125 - 126 ° C
Sublimation	:	
Method	:	
Year	:	1982
GLP	:	
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	Measured value

04.06.2002 (1)

2.2 BOILING POINT

Value	:	= 273 ° C at
Decomposition	:	
Method	:	other: calculated
Year	:	2002
GLP	:	
Test substance	:	

04.06.2002 (2)

2.3 DENSITY

2.3.1 GRANULOMETRY

2.4 VAPOUR PRESSURE

Decomposition		
Method		other (measured)
Year	:	1967
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	0.014 mm Hg at 25 0C

04.06.2002 (3)

2.5 PARTITION COEFFICIENT

Log pow	:	= 3.53 at ° C
Method		other (measured)
Year	:	1967
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4

04.06.2002 (3)

2.6.1 WATER SOLUBILITY

Value	:	= 8.5 mg/l at 25 ° C
Qualitative	:	slightly soluble (0.1-100 mg/L)

Pka	:	at 25 ° C
PH	:	at and ° C
Method	:	other: measured
Year	:	1982
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	Dissociation Constant: Not applicable. Does not ionize within environmentally relevant pH ranges.

04.06.2002 (4)

2.6.2 SURFACE TENSION

2.7 FLASH POINT

2.8 AUTO FLAMMABILITY

2.9 FLAMMABILITY

2.10 EXPLOSIVE PROPERTIES

2.11 OXIDIZING PROPERTIES

2.12 ADDITIONAL REMARKS

3.1.1 PHOTODEGRADATION

Indirect photolysis	
Sensitizer	OH
Conc. of sens.	1500000 molecule/cm3
Rate constant	= .000000000000011 cm3/(molecule*sec)
Degradation	ca. 50 % after 974 day
Source	The Dow Chemical Company, Midland, MI.

05.06.2002 (5)

3.1.2 STABILITY IN WATER

3.1.3 STABILITY IN SOIL

3.2 MONITORING DATA

3.3.1 TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS

3.3.2 DISTRIBUTION

3.4 MODE OF DEGRADATION IN ACTUAL USE

3.5 BIODEGRADATION

3.6 BOD5, COD OR BOD5/COD RATIO

COD		
Method	:	other: ThOD
Year	:	1975
GLP	:	no
COD	:	= .64 mg/g substance

04.06.2002 (6)

3.7 BIOACCUMULATION

3.8 ADDITIONAL REMARKS

4.1 ACUTE/PROLONGED TOXICITY TO FISH

Type	:	flow through
Species	:	Pimephales promelas (Fish, fresh water)
Exposure period	:	96 hour(s)
Unit	:	mg/l
Analytical monitoring	:	no data
LC50	:	c = .47
Method	:	other
Year	:	1985
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4

04.06.2002 (7)

Type	:	static
Species	:	Notropis atherinoides
Exposure period	:	72 hour(s)
Unit	:	mg/l
Analytical monitoring	:	no
LC0	:	m = 1
LC50	:	c = 1.23
LC100	:	m = 2
Method	:	other
Year	:	1972
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Lake Emerald shiners were exposed to 1.0, 1.5, or 2.0 mg/L PCP for 72 hours in dechlorinated Lake Huron water at 50 deg. F. under static conditions.

04.06.2002 (8)

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

Type	:	
Species	:	other aquatic crustacea: sand shrimp
Exposure period	:	43 hour(s)
Unit	:	mg/l
Analytical monitoring	:	no data
EC50	:	= 1.8
Method	:	other
Year	:	1985
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4

04.06.2002 (9)

Type	:	static
Species	:	other: ciliate protozoan, Tetrahymena pyriformis
Exposure period	:	
Unit	:	
Analytical monitoring	:	
Method	:	
Year	:	1989
GLP	:	
Test substance	:	

04.06.2002 (10)

4.3 TOXICITY TO AQUATIC PLANTS E.G. ALGAE

4.4 TOXICITY TO MICROORGANISMS E.G. BACTERIA

4.5.1 CHRONIC TOXICITY TO FISH

4.5.2 CHRONIC TOXICITY TO AQUATIC INVERTEBRATES

4.6.1 TOXICITY TO SOIL DWELLING ORGANISMS

4.6.2 TOXICITY TO TERRESTRIAL PLANTS

4.6.3 TOXICITY TO OTHER NON-MAMM. TERRESTRIAL SPECIES

4.7 BIOLOGICAL EFFECTS MONITORING

4.8 BIOTRANSFORMATION AND KINETICS

4.9 ADDITIONAL REMARKS

5.1.1 ACUTE ORAL TOXICITY

Type	LD50
Species	rat
Strain	Fischer 344
Sex	male
Number of animals	12
Vehicle	other: corn oil
Value	= 435 mg/kg bw
Method	other
Year	1987
GLP	no
Test substance	as prescribed by 1.1 - 1.4
Method	Young adult male rats were fasted overnight. They were administered the material as a solution in corn oil at a dose volume of 10 ml/kg bw at dose levels of 100, 250, 500, or 750 mg/kg bw. Animals were observed closely for two weeks, then submitted for pathological examination. All animals which died prior to scheduled necropsy were also submitted for pathological examination. Body weights were recorded on the day of treatment (Study Day 0), and Study Days 1, 8, and 15.
Result	Acute oral toxicity was characterized as moderate. The acute oral LD50 for male rats was approximately 435 mg/kg, when calculated using the moving average method.

Dose (mg/kg)	Number Treated	Number Dead
100	3	0
250	3	0
500	3	2
750	3	3

In-life signs of toxicity were observed only in rats receiving 500 or 750 mg/kg, and included lethargy, tremors/muscle spasms, lacrimation, palpebral closure, and death on the day of treatment. No clinical evidence of treatment-related effects were seen at 100 or 250 mg/kg. All surviving rats gained weight over the 2-week observation period.

Source	The Dow Chemical Company, Midland, MI.
Reliability	(1) valid without restriction Study conducted in accordance with generally accepted scientific principles. GLP not compulsory at time study was performed.

05.06.2002

Type	:	LD50
Species	:	rat
Strain	:	no data
Sex	:	female
Number of animals	:	3
Vehicle	:	other: rodent chow
Value	:	= 126 - 1000 mg/kg bw
Method	:	other
Year	:	1963
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Source	:	The Dow Chemical Company, Midland, MI
Reliability	:	(2) valid with restrictions

05.06.2002

5.1.2 ACUTE INHALATION TOXICITY

5.1.3 ACUTE DERMAL TOXICITY

5.1.4 ACUTE TOXICITY, OTHER ROUTES

5.2.1 SKIN IRRITATION

Species	:	rabbit
Concentration	:	undiluted
Exposure	:	Occlusive
Exposure time	:	24 hour(s)
Number of animals	:	1
PDII	:	
Result	:	moderately irritating
EC classification	:	
Method	:	other
Year	:	1965
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Neat Material: A male rabbit was prepared by shaving the hair from the entire abdomen with a straight razor and barber soap. The animal was then rested for several days to allow any abrasions to heal completely and to be sure skin was suitable for use. Two sites on the abdomen were used for applications: one intact, the other cross-hatched with a sharp hypodermic needle to penetrate the stratum corneum but not to produce more than a trace of bleeding. Ten applications were made to the intact abdominal site over a period of 14 days. Three consecutive daily applications were made to the abraded site. Both abdominal sites were covered with 1X1 cotton pads and held place with a single cotton cloth taped to remaining body hair. Applications were discontinued upon production of a substantial skin burn, or if the animal died. 10% Dilution in Dowanol* DPM: A male rabbit was prepared by shaving the hair from the entire abdomen with a straight razor and barber soap. The animal was then rested for several days to allow any abrasions to heal completely and to be sure skin was suitable for use. Ten applications (unoccluded) were made to the ear over a period of 14 days. Two sites on the abdomen were used for applications: one intact, the other cross-hatched with a sharp hypodermic needle to penetrate the stratum corneum but not to produce more than a trace of bleeding. Ten applications were made to the intact abdominal site over a period of 14 days. Three consecutive daily applications were made to the abraded site. Both abdominal sites were covered with 1X1 cotton pads and held place with a single cotton cloth taped to remaining body hair. Applications were discontinued upon production of a substantial skin burn, or if the animal died.
Result		Neat Material: At the intact abdominal site, slight to moderate hyperemia and slight edema was observed during the first week of application. Slight necrosis appeared after the 5th application. All signs of irritation resolved within 21 days. Similar results were seen at the abraded abdominal site, with the exception that necrosis was first observed after the 4th application. 10% Dilution in Dowanol* DPM: The site at the rabbit ear had no signs of irritation. Both the intact and abraded abdominal sites had slight to moderate hyperemia and edema appear within the first week. All signs of

irritation resolved within 21 days.

Source The Dow Chemical Company, Midland, MI.
05.06.2002

5.2.2 EYE IRRITATION

Species	:	rabbit
Concentration	:	undiluted
Dose	:	.1 ml
Exposure Time	:	24 hour(s)
Comment	:	
Number of animals	:	1
Result	:	not irritating
EC classification	:	not irritating
Method	:	other
Year	:	1965
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Both eyes of a white rabbit were stained with 5% fluorescein dye and examined for evidence of injury or alterations. The rabbit was then allowed to rest for 24 hours before test. Two drops of the material were introduced into the right eye. The eye was washed within 30 seconds for 2 minutes in a flowing stream of tepid water. Two drops of material were introduced in a similar fashion to the left eye, but this eye was left unwashed. Immmediately after instillation into each eye, the rabbit was examined for signs of discomfort. Within 2-3 minutes after the unwashed eye was treated, each eye was observed for conjunctival and corneal response. Similar observations were made on both eyes at 1 hour, 24 hours, 48 hours, and 6-8 days post-treatment. Examinations were conducted both with and without fluorescein dye.
Result		In both washed and unwashed eyes, the material caused very slight discomfort and very slight conjunctival irritation which resolved within 1 hour.
Source		The Dow Chemical Company, Midland, MI.

05.06.2002 (13)

5.3 SENSITIZATION

Type	:	Split adjuvant test
Species	:	guinea pig
Concentration	:	Induction 5 % intracutaneous Challenge 5 % open epicutaneous
Number of animals	:	8
Vehicle	:	other: Dowanol* DPM/Tween* 80, 9/1
Result	:	sensitizing
Classification	:	
Method	:	other
Year	:	1965
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Source	:	The Dow Chemical Company, Midland, MI.

05.06.2002

5.4 REPEATED DOSE TOXICITY

Species	:	rat
Sex	:	male/female
Strain	:	no data
Route of admin.	:	oral feed
Exposure period	:	90 days
Frequency of treatment	:	continuous
Post obs. period	:	none
Doses	:	0, 0.3, 1, 3, 10, 30 mg/kg/day
Control group	:	yes, concurrent vehicle
NOAEL	:	= 10 mg/kg bw
LOAEL	:	= 30 mg/kg bw
Method	:	other
Year	:	1968
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Groups of 10-15 45-day old rats/sex/dose group were treated with 0, 0.3, 1 3, 10, or 30 mg/kg/day via diet. Rats were randomly assigned to treatment groups. Vehicle for the test material and feed for the controls was Purina ground rodent chow. Diets designed to deliver the nominal dose were mixed weekly on the basis of rat body weight and feed consumption. Body weights and feed consumption were collected once/week for the duration of the study. All animals were observed frequently for clinical signs of toxicity. Blood samples were collected from 5 rats/sex/dose from the 0, 10, and 30 mg/kg/day levels via orbital sinus puncture during weeks 3 and 12, and at termination. Hematological parameters examined included Hgb, crit, RBC, WBC, and differential counts. Blood urea nitrogen determinations were run on 10 rats/sex/dose at termination, and SGPT determinations were run for 5 rats/sex/dose at 0 and 30 mg/kg/day levels on days 1, 3, 7, 14, 30, and termination (10 rats/sex/dose). A complete necropsy examination was conducted on a standard set of tissues, including reproductive organs. Weights were collected for lungs, heart, liver, kidneys, spleen, testes, and brain. In an effort to clarify testicular findings among dosed rats, additional studies were undertaken. Repeated intubation: Groups of 10 male rats/dose were given 0, 62.5, 125, or 250 mg/kg/day via gavage 5 days/week for 2 weeks. Rats were necropsied 3 and 18 days after the last dose Body weights and testicular weights were recorded, and testes, prostate, seminal vesicles, coagulating gland, and epididymis were examined for microscopic lesions. SGPT determinations were conducted at necropsy. Dietary: Groups of 30 male rats were given diets at dose levels of 0, 62.5, 125, or 250 mg/kg/day. 5 rats/dose were necropsied on test days 49, 119, 175, and 242. Body weights and testicular weights were recorded, and testes, prostate, seminal vesicles, coagulating gland, and epididymis were examined for microscopic lesions. Livers were also examined on rats killed on days 175 and 242. SGPT determinations were conducted at necropsy.
Result		There were no treatment-related morphological changes observed at any level in females. Male rats given 30 mg/kg/day had increased relative liver and kidney

weights and mild focal hyaline droplet degeneration of the convoluted tubules of the renal cortex. No histological changes were observed in livers.

Testicular tubal atrophy of varying degrees was observed at all dose levels in the male rats. Not all animals within a dose level were affected, and severity was not dose-related.

In the follow-up studies, no treatment-related differences were observed for final body weight, testicular weight, gross pathology and histopathology. There was a marked degeneration of SGPT values at all dose levels. In the repeated intubation experiment, values were moderately depressed 3 days after final dosing, but returned to normal by the 18 day kill. In the dietary experiment, SGPT values were severely depressed at 49 and 119 days. Values at 175 and 242 days improved, but were still markedly lower than controls. Testicular effects observed in the earlier study could not be replicated, even at these much higher dose levels.

Source The Dow Chemical Company, Midland, MI.
Reliability (2) valid with restrictions
05.06.2002 (14)

Species	:	rat
Sex	:	no data
Strain	:	other: Alderly Park
Route of admin.	:	inhalation
Exposure period	:	6 hours
Frequency of treatment	:	16 exposures
Post obs. period	:	none
Doses	:	saturated vapor; ~1 ppm (0.01 mg/L)
Control group	:	no data specified
NOAEL	:	= 1 ppm
Method	:	other
Year	:	1970
GLP	:	no
Test substance	:	no data
Result	:	No rats died, no toxic signs were observed, and no organs were affected at necropsy.
Source	:	The Dow Chemical Company, Midland, MI.
Reliability	:	(2) valid with restrictions

05.06.2002 (15)

5.5 GENETIC TOXICITY 'IN VITRO'

5.6 GENETIC TOXICITY 'IN VITRO'

5.7 CARCINOGENITY

5.8 TOXICITY TO REPRODUCTION

5.9 DEVELOPMENTAL TOXICITY/TERATOGENICITY

5.10 OTHER RELEVANT INFORMATION

5.11 EXPERIENCE WITH HUMAN EXPOSURE

6. References

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7. Risk Assessment

7.1 END POINT SUMMARY

7.2 HAZARD SUMMARY

7.3 RISK ASSESSMENT